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SECTION A.—SANITARY SCIENCE.

Active and Passive Immunisation Against Common Infectious Diseases, by
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IT is well known that by efficient vaccination one can obtain complete protection against smallpox ; it is not so well known that it is possible to make an immune serum and by injecting this into an unprotected animal show that the serum by " passive immunisation " gives protection against an infection with smallpox virus. Teissier in 1912 showed that the serum of patients convalescent after smallpox was of use in the treatment of cases of smallpox.

The common diseases to which one or another of these methods has been applied are diphtheria, scarlet fever, measles, variola, mumps, whooping cough and varicella.

Early in the history of immunity it was discovered that the serum of an animal which had recovered from an infectious disease contained some protective substance against the infecting agent. It was not long before the blood or serum of people who had recovered from a disease was used for the protection or treatment of those exposed to, or suffering from, the same infection, and this is still the only method open to us in connection with several of the common infectious diseases.

Diphtheria.

For many years we have known that one can cut short an epidemic of diphtheria in an institution by passive immunisation, *i.e.*, by giving antitoxin serum to everyone of the individuals exposed. This method is still used, though it is, not the best way of dealing with an outbreak in a small population.

In England active immunisation has been in use for some three to four years. It is time to ask how it has acted. Dr. Okell, Dr. Parish and I, have had four institutions under our own close observation for practically the whole time, and we are thoroughly satisfied with the results. It is fair to ask and answer a number of questions.

- (1) Has the immunisation caused any harm ? We know of no instance in a total number of some 3,000 people, of whom about one-third have been immunised.

- (2) Has the procedure stopped diphtheria in these institutions? In three of them diphtheria has practically completely disappeared. In the fourth institution, some 600 of the settled population are kept fully immunised, but the "floating population" in and out of the hospital is not immunised. Amongst this latter population 45 cases of diphtheria have been notified during the period of observation. Amongst the immunised population no cases of typical clinical diphtheria have occurred.

In our four years' experience four children known to be Schick negative reactors, developed mild attacks of fever with sore throat, in the swabs from which virulent diphtheria organisms were found. The signs and symptoms resembled those present in some mild attacks of diphtheria, but no toxæmia was present and the clinical picture was not that of indubitable diphtheria. One may, if one wishes, regard these four cases as being mild attacks of diphtheria, or as tonsillitis in carriers of virulent diphtheria organisms.

Even allowing for these four exceptions we feel justified in believing that the chance of a patient, negative to the Schick reaction, suffering from diphtheria is small and that in the rare cases where possibly an infection occurs the attack will be mild.

Our experience in general agrees entirely with that of Park and Zingher and other American workers. We may be allowed to take this opportunity of expressing our deep appreciation of the generous response to any appeals for information, supplies of test material, etc., from American co-workers, particularly Drs. Park and Zingher, the Drs. Dick and Dr. Dochez.

We would again emphasize the point my colleagues and I brought forward last year. We have known of a number of patients who have been considered to have developed "diphtheria," though they had previously given a negative response to the Schick test, but in none of them have we found indubitable clinical diphtheria when the evidence for the negative Schick reaction was impregnable.

With the experience of the past five to ten years, we think that, though in such cases it may be necessary for the clinician to act on a diagnosis of diphtheria in the interest of safety, it will be found when the full bacteriological and immunological data are available, that this diagnosis cannot be confirmed. In such instances, in addition to the full history of the Schick test and of the illness, it is necessary to have a small sample of blood taken immediately before the giving of the first dose of antitoxin, and a swab to be examined for the presence of virulent organisms.

I may, perhaps be allowed here to refer to the handling of an outbreak of diphtheria amongst the population of an institution. We would again call attention to the method we suggested several years ago. We would Schick

test the whole of the inmates and isolate the " Schick negative " " swab positive " people, for it is amongst them that carriers of virulent bacilli are found.

With regard to possible danger from the use of prophylactic, it may be of interest to state that the mixtures we have used for immunisation for a considerable time past have contained formalinised toxin, so called " toxoid " mixed with the requisite quantity of antitoxin. Such mixtures, after freezing and thawing do not become toxic.

Scarlet Fever.

As is well known, a little over a year ago the Drs. Dick in America discovered a test analogous to the Schick test for diphtheria. From the work of the American investigators, particularly the Drs. Dick, Dochez, and Park and Zingher, great progress has been made. Apparently a person giving a positive Dick test is susceptible to scarlet fever and one giving a negative test is immune against scarlet fever.

An interesting observation was made recently in Scotland. Six patients certified as suffering from scarlet fever were admitted. None showed typical scarlet fever, and on being tested all gave a negative response to the Dick test, thus confirming the opinion of the resident medical officer that the patients were not suffering from scarlet fever. The circumstances were such that it was necessary to leave these patients in the scarlet fever ward. None contracted the disease. Eight other people similarly certified and considered not to be suffering from scarlet fever by the resident medical officer were found to be positive to the Dick test, and therefore not immune. Arrangements could not be made for the removal of these patients, and within ten days six of them developed typical scarlet fever obviously caught in the ward.

With the Dick test the story is not so simple as in diphtheria, and there are more exceptions than one would expect.

Thus, practically 100 per cent. of patients suffering from diphtheria, who have not yet been given serum, show a positive response to the Schick test. In England, at all events, we do not yet find 100 per cent. of scarlet fever patients giving a positive Dick response; the percentage is apparently between 60 and 90. The whole investigation is much too young yet to allow of dogmatism, but apparently the test does indicate susceptibility or immunity, and will prove to be of considerable help in dealing with scarlet fever.

Active immunisation is now beginning to be studied in England. The reports from America show that in many hospitals it has become customary to test the whole of the ward personnel and immunise those who give a positive reaction. The results of this procedure seem to show that one can with fair confidence expect scarlet fever amongst the ward personnel to disappear. It is satisfactory to know that even a toxin many times stronger than that used for immunisation has in no instance caused any permanent harm. Thus, even

a grave accidental miscalculation of the strength of the toxin is not likely to cause any serious or permanent harm to the person being immunised.

Passive immunisation.—We find that 5 or 10 c.c. of the horse antitoxin which has been prepared by my colleague, Dr. Okell, against the scarlet fever streptococcus, will cause a positive Dick reactor to become negative in a few hours time. It is practically certain that with this change an immunity of reasonably high degree is conferred on the patient. In this way ward outbreaks can presumably be cut short at once.

The serum has also been used in many hospitals for treatment, but that is not the subject we are discussing to-day. I may be allowed to say that the results are promising and in many instances very favourable. We must, however, wait until a large number of cases have been treated before we can make up our minds that scarlet fever antitoxin is efficient in the treatment of the disease. I have little doubt that it will be effective, but one must keep an open mind until the evidence establishes or negatives the value of the antitoxin.

Measles.

So far, no satisfactory means of immunisation against measles has been tried on a large scale. From many points of view, active immunisation is much to be preferred to passive. I have found in an American article an extraordinarily interesting account of the first traceable attempt to immunise people actively against measles. Apparently this city of Edinburgh was in 1759, as now, in the forefront of practical immunology, for in that year Francis Home here made an investigation in the course of which he took blood from the superficial veins in the eruptive areas, soaked wool swabs in the blood and with them rubbed scarified areas in the skin of children who had not yet had measles.

His careful records enable one to-day to trace with considerable accuracy what occurred. Though he thought he produced mild and modified measles, it is very doubtful if he produced the real disease in any instance. But the thought and principle underlying his action is curiously near to the theories of modern immunology.

Herrman in America in 1923, brought forward a plan for immunising all infants during the fourth and fifth months of life. At this time most infants are passively immune against measles, having received maternal immunity in utero. Herrman decided to apply nasal mucous, centrifuged clear of bacteria, to the mucous membrane of children four to five months old when they were still protected against a severe attack of the disease by the residual maternal antitoxin still in their blood. In this way he obtained the action of virus-serum mixture in the infant just as in diphtheria we use a toxin antitoxin mixture. I have seen no late reports of the method, but believe it is still being used under certain circumstances.

Zingher (Journ. Amer. Med. Assoc., 1924, 82, 1180), prefers to give to children who have been unwittingly exposed to infection with measles, a very small dose of serum taken from a patient convalescent after the disease. This small dose of serum is sufficient to protect the infant from a full attack of measles, but a minor infection develops and the child, without risk, thereafter is immune. This method has not yet been tried on a large scale, but it may be of very great use in certain conditions. In Italy, Caronia and Sindoni have used a vaccine from which they have seen good results. The method has not yet been generally accepted.

Passive protection can be given. Weisbecker reported some favourable results in 1899 from the use of convalescent serum. In 1916, Nicolle and Conseil used convalescent measles serum in Algiers, as did Park and Zingher in the same year; later Degkwitz, in Munich, strongly advocated the procedure. These workers all found that the serum of patients convalescent after an attack of measles will protect children exposed to the disease, or when given to patients ill of the disease will cause improvement.

The method is widely used in Germany and America. Convalescent patients known to give a negative Wassermann test and considered to be free of active tubercle are asked to give a small supply of blood, the serum is drawn off, and stored in phials until required either to protect children unwittingly exposed to the disease or for the treatment of severe cases of the disease. Even though on the Continent and in America special clinics have been established to arrange for supplies of this serum, it is obvious that under present social conditions such a method could have but a limited application. But anyone who has seen in his own family what a dangerous disease measles can be, and what an amount of trouble and expense it can cause to a small school population in which an outbreak has occurred, will be inclined to make very determined efforts to obtain supplies of serum from patients recently convalescent or from adults, relatives or others, who are known to have suffered from the disease.

One is always hoping that it may become possible to make an effective serum for protection against, or treatment of, this disease. There are indications in the work of the last year or two that one's hopes may be justified in the not distant future.

Mumps.

Regan, in America, and other workers, have used the serum of patients convalescent from mumps for the protection of people who have been exposed to infection. In the absence of convalescent serum, Regan advocates taking 20 or 30 c.c. of blood from the mother or father and injecting it at once intramuscularly into the child it is desired to protect. Apparently the method is successful, but it has not yet been very widely used.

Whooping Cough.

Debré and other French workers have used the serum of convalescent patients or the blood of parents for the protection of children already exposed to infection and also for the treatment of those already "whooping." Apparently a satisfactory protection is obtained ; in patients already suffering severely from the disease, the general condition is greatly relieved, and the liability to complication lessened, but the cough is slightly influenced, if at all

Varicella.

Z. von Barabas has used the serum of convalescent patients in order to protect children exposed to this disease. The results were promising.

In conclusion, one can hardly visualise the time when every infant "born into this world alive," before it can decide which political party it will adopt, will spend several happy months in being immunised against half a dozen of the dangerous infectious diseases of childhood. But we can wait for that difficulty to be dealt with when we are competent to produce universal immunity—meanwhile we may remember that for the past ten or twenty years diphtheria has caused England never less than 1,300 deaths per annum, whooping cough never less than 4,000 and measles never less than 5,000 deaths a year, and that it is probable that the physician dealing with a child already exposed to, or beginning to suffer from, any one of these diseases, has at hand in the mother and father a potential source of blood containing a certain quantity of anti-toxin which can be easily and safely given as whole blood intramuscularly to the threatened or ailing infant.

